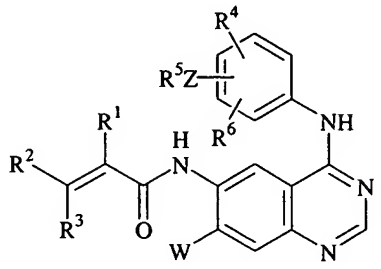
WHAT IS CLAIMED IS:

1. A method of making a compound of Formula 1,



1

or a pharmaceutically acceptable salt, ester, amide or prodrug thereof, in which

R^1, R^2 and R^3 are independently hydrogen, halogen, NO_2, CN, CF_3, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-8} cycloalkyl, C_{3-8} heterocyclyl, carboxy, C_{1-6} alkoxycarbonyl, C_{1-6} alkylcarbamoyl, aryl-$(CH_2)_m$, heteroaryl-$(CH_2)_m$, heterocyclyl-$(CH_2)_m$, $(CH_2)_mCO_2R^8$, $(CH_2)_mS(O)_nR^8$, $(CH_2)_mSO_2NR^8R^9$, OR^8, SR^8, $(CH_2)_mNR^8R^9$, $(CH_2)_mN(O)R^8R^9$, $(CH_2)_mP(O)(OR^8)(OR^9)$, $(CH_2)_mCOR^8$, $(CH_2)_mCO_2R^8$, $(CH_2)_mC(O)NR^8R^9$, $(CH_2)_mC(O)NR^8SO_2R^8$, $(CH_2)_mNR^8SO_2R^9$, $(CH_2)_mC(O)NR^8OR^9$, $(CH_2)_mS(O)_nR^8$, or $(CH_2)_mSO_2NR^8R^9$, wherein aryl-$(CH_2)_m$ includes phenylalkyl or substituted phenylalkyl having from one to three substituents that are independently NO_2, CN, CF_3, C_{1-6} alkyl-NH, $(C_{1-6}$ alkyl$)_2N$, or monocyclic heteroaryl, and each C_{1-6} alkyl is optionally substituted with OH, NH_2 or -N(A)B;

R^4 and R^6 are independently hydrogen, hydroxy, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkylamino, C_{1-4} alkyldiamino, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylcarbonyl, C_{1-4} alkylcarbamoyl, dicarbamoyl, carbamyl, C_{1-4} alkoxycarbonyl, cyano, nitro, or trifluoromethyl;

R^5 is phenyl, pyridyl, furyl, thiazolyl, imidazolyl or thienyl, each optionally having one or two substituents that are independently halogen, C_{1-6} alkyl, C_{1-6} alkoxy, hydroxy, amino, cyano, C_{1-6} alkyl-NH or $(C_{1-6}$ alkyl$)_2N$;

W is SR^7, OR^7 or NHR^7; and

Z is hydrogen, halogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{1-6} alkoxy, C_{3-8} cycloalkoxy, nitro, C_{1-6} haloalkyl, hydroxy, C_{1-6} acyloxy, NH_2, C_{1-6} alkyl-NH, $(C_{1-6}$ alkyl$)_2N$, C_{3-8} cycloalkyl-NH, $(C_{3-8}$ cycloalkyl$)_2N$, hydroxymethyl, C_{1-6} alkylcarbonyl, cyano, azido, C_{1-6} thioalkyl, C_{1-6} sulfinylalkyl, C_{1-6} sulfonylalkyl, C_{3-8} thiocycloalkyl, C_{3-8} sulfinylcycloalkyl, C_{3-8} sulfonylcycloalkyl, mercapto, C_{1-6} alkoxycarbonyl, C_{3-8} cycloalkoxycarbonyl, C_{2-4} alkenyl, C_{4-8} cycloalkenyl, or C_{2-4} alkynyl, provided that when Z is monovalent, R^5 is absent;

wherein, R^7 is hydrogen, C_{1-6} alkyl, piperidin-1-yl-$(CH_2)_m$, piperazin-1-yl-$(CH_2)_m$, 4-C_{1-6} alkyl-piperazin-1-yl-$(CH_2)_m$, pyrrolidin-1-yl-$(CH_2)_m$, pyridinyl-$(CH_2)_m$, imidazolyl-$(CH_2)_m$, imidazol-1-yl-$(CH_2)_m$, morpholin-4-yl-$(CH_2)_m$, thiomorpholin-4-yl-$(CH_2)_m$, or hexahydroazepin-1-yl-$(CH_2)_m$, wherein each C_{1-6} alkyl optionally includes one or more substituents that are OH, NH_2 or -N(A)B;

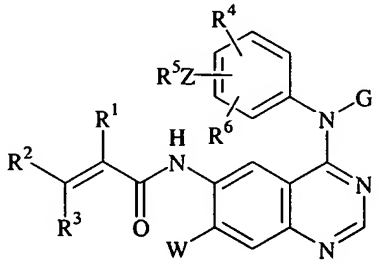
R^8 and R^9 are each independently hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, arylalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, or heteroarylalkyl;

A and B are independently hydrogen, C_{1-6} alkyl, $(CH_2)_mOH$, piperidin-1-yl-$(CH_2)_m$, piperazin-1-yl-$(CH_2)_m$, 4-C_{1-6} alkyl-piperazin-1-yl-$(CH_2)_m$, pyrrolidin-1-yl-$(CH_2)_m$, pyridinyl-$(CH_2)_m$, imidazolyl-$(CH_2)_m$, or imidazol-1-yl-$(CH_2)_m$; and

n and m are, respectively, integers from zero to two, inclusive, and from zero to four, inclusive;

the method comprising:

removing a protecting group, G, from a compound of Formula 10,

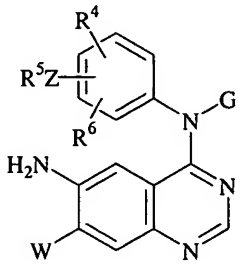


10

to yield the compound of Formula 1; and

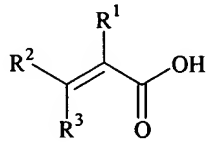
optionally converting the compound of Formula 1 to a pharmaceutically acceptable salt, ester, amide or prodrug thereof.

2. The method of claim 1, further comprising reacting a compound of Formula 7,



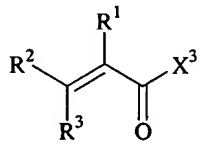
7

with a compound of Formula 8,



8

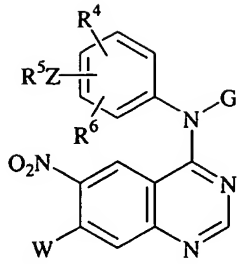
or with a compound of Formula 9,



9

to yield the compound of Formula 10, wherein G, R^1, R^2, R^3, R^4, R^5, R^6, W, and Z are as defined in claim 1, X^3 is a leaving group, and provided that when G is Boc, W is not alkoxy.

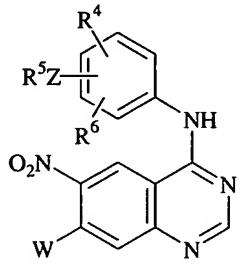
3. The method of claim 2, further comprising reacting a compound of Formula 6,



6

with hydrogen in the presence of a catalyst or with a reducing agent to yield the compound of claim 7, wherein G, R^4, R^5, R^6, W, and Z are as defined in claim 1.

4. The method of claim 3, further comprising installing the protecting group, G, on a compound of Formula 5,



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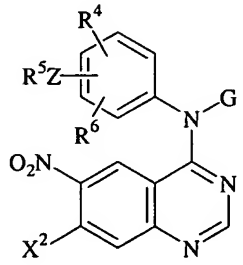
to yield the compound of Formula 6, wherein G, R^4, R^5, R^6, W, and Z are as defined in claim 1.

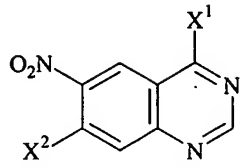
5. The method of claim 3, further comprising displacing a leaving group, X^2, of Formula 12,



12

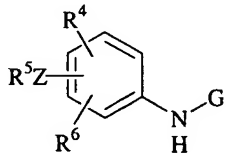
with W to yield the compound of Formula 6, wherein G, R^4, R^5, R^6, W, and Z are as defined in claim 1, and provided that when G is Boc, X^2 is not halogen.

6. The method of claim 5, further comprising reacting a compound of Formula 2,



2

with a compound of Formula 11,



11

to yield the compound of Formula 12, wherein G, R^4, R^5, R^6, and Z are as defined in claim 1, X^2 is as defined in claim 5, and X^1 is a leaving group.

7. The method of claim 1, wherein G is acetyl.

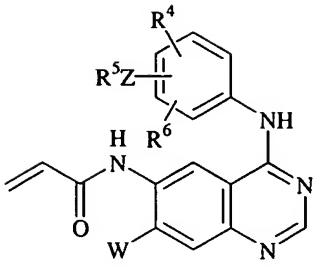
8. The method of claim 1, wherein G is dimethoxy benzyl.

9. The method of claim 1, wherein R^1, R^2, R^3 and Z are each hydrogen, and R^4 and R^6 are each halogen.

10. The method of claim 1, wherein W is morpholin-4-yl-alkoxy.

11. The method of claim 1, wherein the compound of Formula 1 is *N*-[4-(3-chloro-4-fluoro-phenylamino)-7-(3-morpholin-4-yl-propoxy)-quinazolin-6-yl]-acrylamide.

12. A method of making a compound of Formula 23,



or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof, in which

R^4 and R^6 are independently hydrogen, hydroxy, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkylamino, C_{1-4} alkyldiamino, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylcarbonyl, C_{1-4} alkylcarbamoyl, dicarbamoyl, carbamyl, C_{1-4} alkoxycarbonyl, cyano, nitro, or trifluoromethyl;

R^5 is phenyl, pyridyl, furyl, thiazolyl, imidazolyl or thienyl, each optionally having one or two substituents that are independently halogen, C_{1-6} alkyl, C_{1-6} alkoxy, hydroxy, amino, cyano, C_{1-6} alkyl-NH or $(C_{1-6}$ alkyl$)_2N$;

W is SR^7, OR^7 or NHR^7; and

Z is hydrogen, halogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{1-6} alkoxy, C_{3-8} cycloalkoxy, nitro, C_{1-6} haloalkyl, hydroxy, C_{1-6} acyloxy, NH_2, C_{1-6} alkyl-NH, $(C_{1-6}$ alkyl$)_2N$, C_{3-8} cycloalkyl-NH, $(C_{3-8}$ cycloalkyl$)_2N$, hydroxymethyl, C_{1-6} alkylcarbonyl, cyano, azido, C_{1-6} thioalkyl, C_{1-6} sulfinylalkyl, C_{1-6} sulfonylalkyl, C_{3-8} thiocycloalkyl, C_{3-8} sulfinylcycloalkyl, C_{3-8} sulfonylcycloalkyl, mercapto, C_{1-6} alkoxycarbonyl, C_{3-8} cycloalkoxycarbonyl, C_{2-4} alkenyl, C_{4-8} cycloalkenyl, or C_{2-4} alkynyl, provided that when Z is monovalent, R^5 is absent;

wherein, R^7 is hydrogen, C_{1-6} alkyl, piperidin-1-yl-$(CH_2)_m$, piperazin-1-yl-$(CH_2)_m$, 4-C_{1-6} alkyl-piperazin-1-yl-$(CH_2)_m$, pyrrolidin-1-yl-$(CH_2)_m$, pyridinyl-$(CH_2)_m$, imidazolyl-$(CH_2)_m$, imidazol-1-yl-$(CH_2)_m$, morpholin-4-yl-$(CH_2)_m$, thiomorpholin-4-yl-$(CH_2)_m$, or hexahydroazepin-1-yl-$(CH_2)_m$, wherein each C_{1-6} alkyl optionally includes one or more substituents that are OH, NH_2 or -N(A)B;

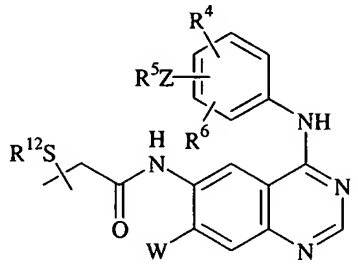
A and B are independently hydrogen, C_{1-6} alkyl, $(CH_2)_mOH$, piperidin-1-yl-$(CH_2)_m$, piperazin-1-yl-$(CH_2)_m$, 4-C_{1-6} alkyl-piperazin-1-yl-$(CH_2)_m$, pyrrolidin-1-

yl-$(CH_2)_m$, pyridinyl-$(CH_2)_m$, imidazolyl-$(CH_2)_m$, or imidazol-1-yl-$(CH_2)_m$; and

m is an integer from zero to four, inclusive;

the method comprising:

eliminating SR^{12} from a compound of Formula 22,

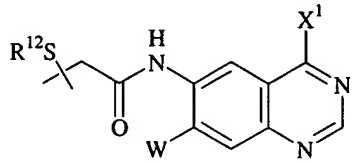


22

to yield the compound of Formula 23; and

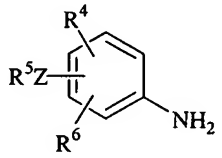
optionally converting the compound of Formula 23 to a pharmaceutically acceptable salt, ester, amide, or prodrug thereof, wherein R^{12} is C_{1-6} alkyl or aryl.

13. The method of claim 12, further comprising reacting a compound of Formula 21,



21

with a compound of Formula 3,



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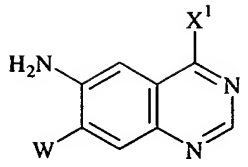
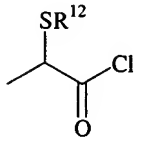
to yield the compound of Formula 22, wherein R^4, R^5, R^6, R^{12}, W, and Z are as defined in claim 12, and X^1 is a leaving group.

14. The method of claim 13, further comprising reacting a compound of Formula 18,



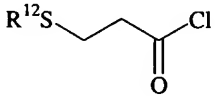
18

with a compound of Formula 19,



19

or with a compound of Formula 20,



20

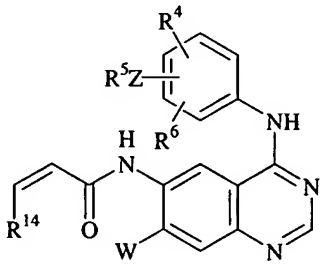
to yield the compound of Formula 21, wherein R^{12} and W are as defined in claim 12, and X^1 is as defined in claim 13.

15. The method of claim 12, wherein Z is hydrogen, and R^4 and R^6 are each halogen.

16. The method of claim 12, wherein W is morpholin-4-yl-alkoxy.

17. The method of claim 12, wherein the compound of Formula 23 is *N*-[4-(3-chloro-4-fluoro-phenylamino)-7-(3-morpholin-4-yl-propoxy)-quinazolin-6-yl]-acrylamide.

18. A method of making a compound of Formula 29,



29

or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof, in which

R^4 and R^6 are independently hydrogen, hydroxy, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkylamino, C_{1-4} alkyldiamino, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylcarbonyl, C_{1-4} alkylcarbamoyl, dicarbamoyl, carbamyl, C_{1-4} alkoxycarbonyl, cyano, nitro, or trifluoromethyl;

R^5 is phenyl, pyridyl, furyl, thiazolyl, imidazolyl or thienyl, each optionally having one or two substituents that are independently halogen, C_{1-6} alkyl, C_{1-6} alkoxy, hydroxy, amino, cyano, C_{1-6} alkyl-NH or $(C_{1-6}$ alkyl$)_2N$;

W is SR^7, OR^7 or NHR^7;

Z is hydrogen, halogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{1-6} alkoxy, C_{3-8} cycloalkoxy, nitro, C_{1-6} haloalkyl, hydroxy, C_{1-6} acyloxy, NH_2, C_{1-6} alkyl-NH, $(C_{1-6}$ alkyl$)_2N$, C_{3-8} cycloalkyl-NH, $(C_{3-8}$ cycloalkyl$)_2N$, hydroxymethyl, C_{1-6} alkylcarbonyl, cyano, azido, C_{1-6} thioalkyl, C_{1-6} sulfinylalkyl, C_{1-6} sulfonylalkyl, C_{3-8} thiocycloalkyl, C_{3-8} sulfinylcycloalkyl, C_{3-8} sulfonylcycloalkyl, mercapto, C_{1-6} alkoxycarbonyl, C_{3-8} cycloalkoxycarbonyl, C_{2-4} alkenyl, C_{4-8} cycloalkenyl, or C_{2-4} alkynyl, provided that when Z is monovalent, R^5 is absent; and

R^{14} is hydrogen, halogen, C_{2-6} alkenyl, C_{2-6} alkynyl, and C_{2-6} alkenyl or C_{2-6} alkynyl substituted with hydroxy, alkoxy, amino or alkylamino;

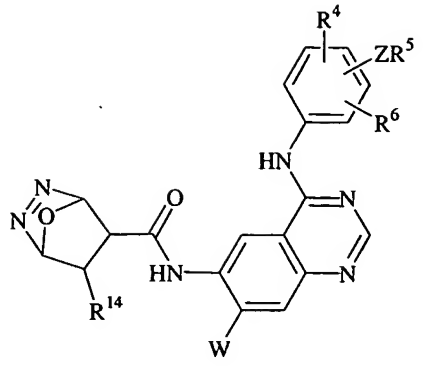
wherein, R^7 is hydrogen, C_{1-6} alkyl, piperidin-1-yl-$(CH_2)_m$, piperazin-1-yl-$(CH_2)_m$, 4-C_{1-6} alkyl-piperazin-1-yl-$(CH_2)_m$, pyrrolidin-1-yl-$(CH_2)_m$, pyridinyl-$(CH_2)_m$, imidazolyl-$(CH_2)_m$, imidazol-1-yl-$(CH_2)_m$, morpholin-4-yl-$(CH_2)_m$, thiomorpholin-4-yl-$(CH_2)_m$, or hexahydroazepin-1-yl-$(CH_2)_m$, wherein each C_{1-6} alkyl optionally includes one or more substituents that are OH, NH_2 or -N(A)B;

A and B are independently hydrogen, C_{1-6} alkyl, $(CH_2)_mOH$, piperidin-1-yl-$(CH_2)_m$, piperazin-1-yl-$(CH_2)_m$, 4-C_{1-6} alkyl-piperazin-1-yl-$(CH_2)_m$, pyrrolidin-1-yl-$(CH_2)_m$, pyridinyl-$(CH_2)_m$, imidazolyl-$(CH_2)_m$, or imidazol-1-yl-$(CH_2)_m$; and

m is an integer from zero to four, inclusive;

the method comprising:

removing [1,3,4]oxadiazole from a compound of Formula 28,

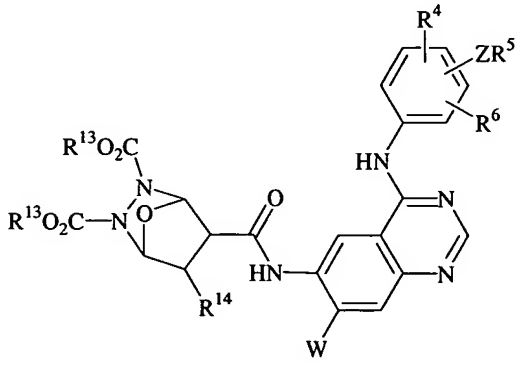


28

to yield the compound of Formula 29; and

optionally converting the compound of Formula 29 to a pharmaceutically acceptable salt, ester, amide, or prodrug thereof.

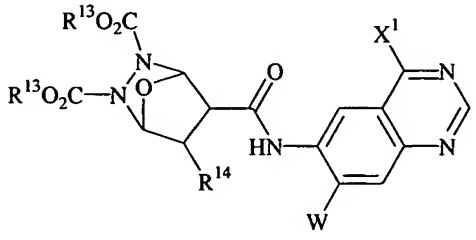
19. The method of claim 18, further comprising removing ester moieties, $R^{13}O_2C$, from a compound of Formula 27,



27

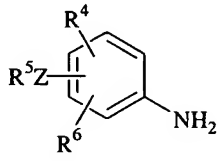
to yield the compound of Formula 28, wherein R^4, R^5, R^6, R^{14}, W, and Z are as defined in claim 18, and R^{13} is C_{1-4} alkyl, C_{1-4} haloalkyl, C_{2-4} alkenyl, TMS-$(CH_2)_m$ or aryl-$(CH_2)_m$.

20. The method of claim 19, further comprising reacting a compound of Formula 26,



26

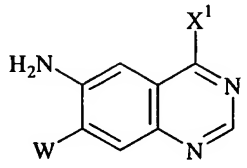
with a compound of Formula 3,



3

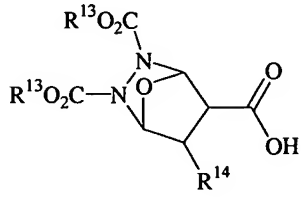
to yield the compound of Formula 27, wherein R^4, R^5, R^6, R^{14}, W, and Z are as defined in claim 18, R^{13} is as defined in claim 19, and X^1 is a leaving group.

21. The method of claim 20, further comprising reacting a compound of Formula 18,



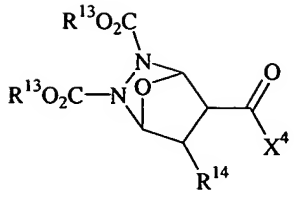
18

with a compound of Formula 24



24

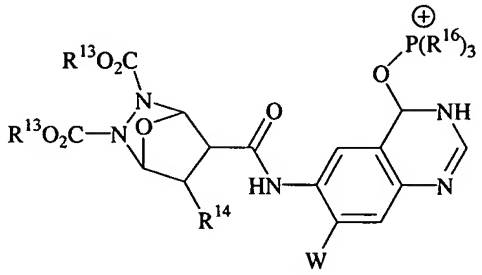
or with a compound of Formula 25



25

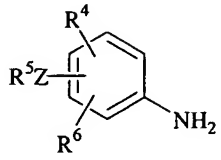
to yield the compound of Formula 26, wherein R^{14} and W are as defined in claim 18, R^{13} is as defined in claim 19, X^1 is as defined in claim 20, and X^4 is a leaving group.

22. The method of claim 19, further comprising reacting a compound of Formula 36,



36

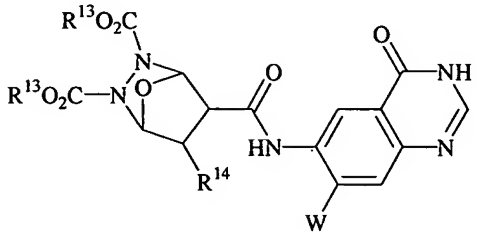
with a compound of Formula 3,



3

to yield the compound of Formula 27, wherein R^4, R^5, R^6, R^{14}, W, and Z are as defined in claim 18, R^{13} is as defined in claim 19, and R^{16} is C_{1-6} alkyl, phenyl, or phenoxy.

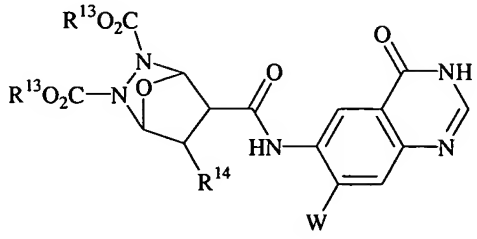
23. The method of claim 22, further comprising reacting a compound of Formula 34



34

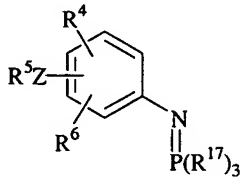
with $(R^{16})_3P(X^5)_2$ to yield the compound of 36, wherein R^{14} and W are as defined in claim 18, R^{13} is as defined in claim 19, R^{16} is as defined in claim 22, and X^5 is hydrogen, halogen or absent.

24. The method of claim 19, further comprising reacting a compound of Formula 34,



34

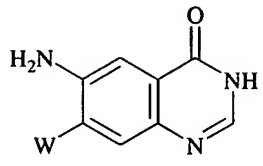
with a compound of Formula 37,



37

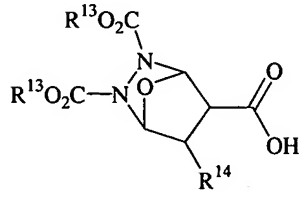
to yield the compound of Formula 27, wherein R^4, R^5, R^6, R^{14}, W, and Z are as defined in claim 18, R^{13} is as defined in claim 19, and R^{17} is $C_{1\text{-}6}$ alkyl, phenyl or phenoxy.

25. The method of claim 24, further comprising reacting a compound of Formula 33,



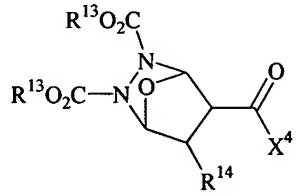
33

with a compound of Formula 24,



24

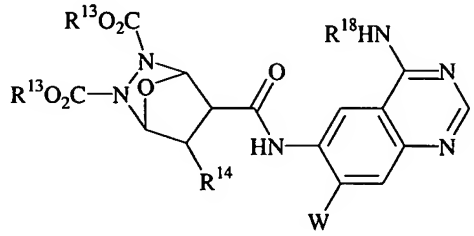
or with a compound of Formula 25,



25

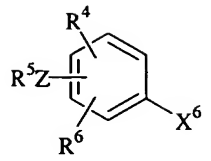
to yield the compound of Formula 34, wherein R^{14} and W are as defined in claim 18, R^{13} is as defined in claim 19, and X^4 is a leaving group.

26. The method of claim 19, further comprising reacting a compound of Formula 38,



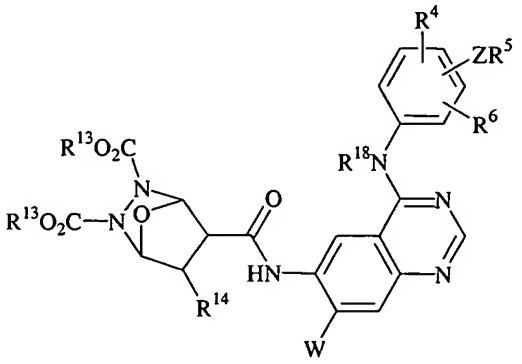
38

with a compound of Formula 39,



39

in the presence of a catalyst to yield a compound of Formula 40,



40

wherein R^4, R^5, R^6, R^{14}, W, and Z are as defined in claim 18, R^{13} is as defined in claim 19, X^6 is halogen, and R^{18} is hydrogen or a group that facilitates coupling of the compounds of Formula 38 and Formula 39; and

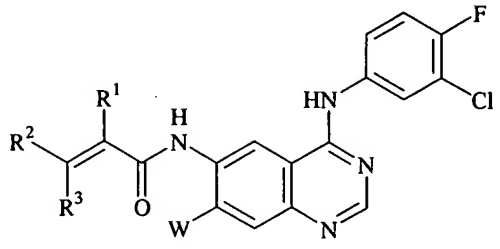
optionally reacting the compound of Formula 40 with an acid to yield the compound of Formula 27 when R^{18} is non-hydrogen.

27. The method of claim 18, wherein Z and R^{14} are each hydrogen, and R^4 and R^6 are each halogen.

28. The method of claim 18, wherein W is morpholin-4-yl-alkoxy.

29. The method of claim 18, wherein the compound of Formula 29 is *N*-[4-(3-chloro-4-fluoro-phenylamino)-7-(3-morpholin-4-yl-propoxy)-quinazolin-6-yl]-acrylamide.

30. A method of making a compound of Formula 46,



46

or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof, in which

R^1, R^2 and R^3 are independently hydrogen, halogen, NO_2, CN, CF_3, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-8} cycloalkyl, C_{3-8} heterocyclyl, carboxy, C_{1-6} alkoxycarbonyl, C_{1-6} alkylcarbamoyl, aryl-$(CH_2)_m$, heteroaryl-$(CH_2)_m$, heterocyclyl-$(CH_2)_m$, $(CH_2)_mCO_2R^8$, $(CH_2)_mS(O)_nR^8$, $(CH_2)_mSO_2NR^8R^9$, OR^8, SR^8, $(CH_2)_mNR^8R^9$, $(CH_2)_mN(O)R^8R^9$, $(CH_2)_mP(O)(OR^8)(OR^9)$, $(CH_2)_mCOR^8$, $(CH_2)_mCO_2R^8$, $(CH_2)_mC(O)NR^8R^9$, $(CH_2)_mC(O)NR^8SO_2R^8$, $(CH_2)_mNR^8SO_2R^9$, $(CH_2)_mC(O)NR^8OR^9$, $(CH_2)_mS(O)_nR^8$, or $(CH_2)_mSO_2NR^8R^9$, wherein aryl-$(CH_2)_m$ includes phenylalkyl or substituted phenylalkyl having from one to three substituents that are independently NO_2, CN, CF_3, C_{1-6} alkyl-NH, $(C_{1-6}$ alkyl$)_2N$, or monocyclic heteroaryl, and each C_{1-6} alkyl is optionally substituted with OH, NH_2 or -N(A)B; and

W is SR^7, OR^7 or NHR^7;

wherein, R^7 is hydrogen, C_{1-6} alkyl, piperidin-1-yl-$(CH_2)_m$, piperazin-1-yl-$(CH_2)_m$, 4-C_{1-6} alkyl-piperazin-1-yl-$(CH_2)_m$, pyrrolidin-1-yl-$(CH_2)_m$, pyridinyl-$(CH_2)_m$, imidazolyl-$(CH_2)_m$, imidazol-1-yl-$(CH_2)_m$, morpholin-4-yl-$(CH_2)_m$, thiomorpholin-4-yl-$(CH_2)_m$, or hexahydroazepin-1-yl-$(CH_2)_m$, wherein each C_{1-6} alkyl optionally includes one or more substituents that are OH, NH_2 or -N(A)B;

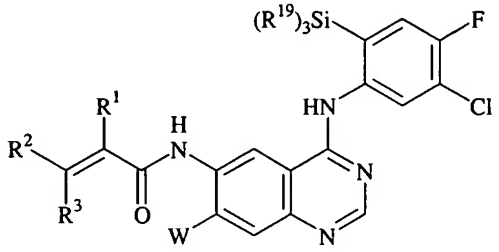
R^8 and R^9 are each independently hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, arylalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, or heteroarylalkyl;

A and B are independently hydrogen, C_{1-6} alkyl, $(CH_2)_mOH$, piperidin-1-yl-$(CH_2)_m$, piperazin-1-yl-$(CH_2)_m$, 4-C_{1-6} alkyl-piperazin-1-yl-$(CH_2)_m$, pyrrolidin-1-yl-$(CH_2)_m$, pyridinyl-$(CH_2)_m$, imidazolyl-$(CH_2)_m$, or imidazol-1-yl-$(CH_2)_m$; and

n and m are, respectively, integers from zero to two, inclusive, and from zero to four, inclusive;

the method comprising:

treating a compound of Formula 45,



45

with an acid to yield the compound of Formula 46, wherein R^{19} is C_{1-4} alkyl, C_{1-4} alkoxy or aryl; and

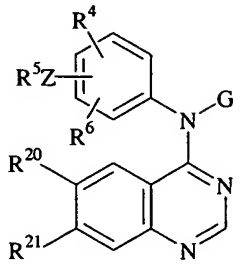
optionally converting the compound of Formula 46 to a pharmaceutically acceptable salt, ester, amide, or prodrug thereof.

31. The method of claim 30, wherein R^1, R^2 and R^3 are each hydrogen.

32. The method of claim 30, wherein W is morpholin-4-yl-alkoxy.

33. The method of claim 30, wherein the compound of Formula 46 is *N*-[4-(3-chloro-4-fluoro-phenylamino)-7-(3-morpholin-4-yl-propoxy)-quinazolin-6-yl]-acrylamide.

34. A compound of Formula 47,



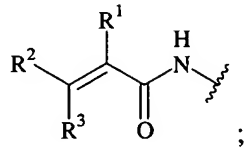
47

or a pharmaceutically acceptable salt, ester, amide or prodrug thereof, in which

R^4 and R^6 are independently hydrogen, hydroxy, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkylamino, C_{1-4} alkyldiamino, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylcarbonyl, C_{1-4} alkylcarbamoyl, dicarbamoyl, carbamyl, C_{1-4} alkoxycarbonyl, cyano, nitro, or trifluoromethyl;

R^5 is phenyl, pyridyl, furyl, thiazolyl, imidazolyl or thienyl, each optionally having one or two substituents that are independently halogen, C_{1-6} alkyl, C_{1-6} alkoxy, hydroxy, amino, cyano, C_{1-6} alkyl-NH or $(C_{1-6}$ alkyl$)_2N$;

R^{20} is NH_2, NO_2, or



;

R^{21} is SR^7, OR^7, NHR^7 or a leaving group;

Z is hydrogen, halogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{1-6} alkoxy, C_{3-8} cycloalkoxy, nitro, C_{1-6} haloalkyl, hydroxy, C_{1-6} acyloxy, NH_2, C_{1-6} alkyl-NH, $(C_{1-6}$ alkyl$)_2N$, C_{3-8} cycloalkyl-NH, $(C_{3-8}$ cycloalkyl$)_2N$, hydroxymethyl, C_{1-6} alkylcarbonyl, cyano, azido, C_{1-6} thioalkyl, C_{1-6} sulfinylalkyl, C_{1-6} sulfonylalkyl, C_{3-8} thiocycloalkyl, C_{3-8} sulfinylcycloalkyl, C_{3-8} sulfonylcycloalkyl, mercapto, C_{1-6} alkoxycarbonyl, C_{3-8} cycloalkoxycarbonyl, C_{2-4} alkenyl, C_{4-8} cycloalkenyl, or C_{2-4} alkynyl, provided that when Z is monovalent, R^5 is absent; and

G is a protecting group, provided that when G is Boc and R^{20} is NH_2 or NO_2, R^{21} is not halogen or alkoxy;

wherein R^1, R^2 and R^3 are independently hydrogen, halogen, NO_2, CN, CF_3, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-8} cycloalkyl, C_{3-8} heterocyclyl, carboxy, C_{1-6} alkoxycarbonyl, C_{1-6} alkylcarbamoyl, aryl-$(CH_2)_m$, heteroaryl-$(CH_2)_m$, heterocyclyl-$(CH_2)_m$, $(CH_2)_mCO_2R^8$, $(CH_2)_mS(O)_nR^8$, $(CH_2)_mSO_2NR^8R^9$, OR^8, SR^8, $(CH_2)_mNR^8R^9$, $(CH_2)_mN(O)R^8R^9$, $(CH_2)_mP(O)(OR^8)(OR^9)$, $(CH_2)_mCOR^8$, $(CH_2)_mCO_2R^8$, $(CH_2)_mC(O)NR^8R^9$, $(CH_2)_mC(O)NR^8SO_2R^8$, $(CH_2)_mNR^8SO_2R^9$, $(CH_2)_mC(O)NR^8OR^9$, $(CH_2)_mS(O)_nR^8$, or $(CH_2)_mSO_2NR^8R^9$, wherein aryl-$(CH_2)_m$ includes phenylalkyl or substituted phenylalkyl having from one to three substituents that are independently NO_2, CN, CF_3, C_{1-6} alkyl-NH, $(C_{1-6}$ alkyl$)_2N$, or monocyclic heteroaryl, and each C_{1-6} alkyl is optionally substituted with OH, NH_2 or -N(A)B;

R^7 is hydrogen, C_{1-6} alkyl, piperidin-1-yl-$(CH_2)_m$, piperazin-1-yl-$(CH_2)_m$, 4-C_{1-6} alkyl-piperazin-1-yl-$(CH_2)_m$, pyrrolidin-1-yl-$(CH_2)_m$, pyridinyl-$(CH_2)_m$, imidazolyl-$(CH_2)_m$, imidazol-1-yl-$(CH_2)_m$, morpholin-4-yl-$(CH_2)_m$, thiomorpholin-4-yl-$(CH_2)_m$, or hexahydroazepin-1-yl-$(CH_2)_m$, wherein each C_{1-6} alkyl optionally includes one or more substituents that are OH, NH_2 or -N(A)B;

R^8 and R^9 are each independently hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, arylalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, or heteroarylalkyl;

A and B are independently hydrogen, C_{1-6} alkyl, $(CH_2)_mOH$, piperidin-1-yl-$(CH_2)_m$, piperazin-1-yl-$(CH_2)_m$, 4-C_{1-6} alkyl-piperazin-1-yl-$(CH_2)_m$, pyrrolidin-1-yl-$(CH_2)_m$, pyridinyl-$(CH_2)_m$, imidazolyl-$(CH_2)_m$, or imidazol-1-yl-$(CH_2)_m$; and

n and m are, respectively, integers from zero to two, inclusive, and from zero to four, inclusive.

35. The compound of claim 34, wherein G is acetyl.

36. The compound of claim 34, wherein G is dimethoxy benzyl.

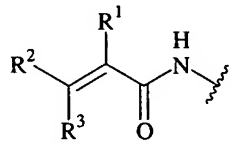
37. The compound of claim 34, wherein R^{20} is NH_2.

38. The compound of claim 37, wherein R^{21} is SR^7, OR^7 or NHR^7.

39. The compound of claim 34, wherein R^{20} is NO_2.

40. The compound of claim 39, wherein R^{21} is SR^7, OR^7 or NHR^7.

41. The compound of claim 34, wherein R^{20} is



42. The compound of claim 41, wherein R^1, R^2, R^3 and Z are each hydrogen, and R^4 and R^6 are each halogen.

43. The compound of claim 34, wherein R^{21} is morpholin-4-yl-alkoxy.

44. A compound selected from:

(3-chloro-4-fluoro-phenyl)-(3,4-dimethoxy-benzyl)-(7-fluoro-6-nitro-quinazolin-4-yl)-amine;

(3-chloro-4-fluoro-phenyl)-(3,4-dimethoxy-benzyl)-[7-(3-morpholin-4-yl-propoxy)-6-nitro-quinazolin-4-yl]-amine;

*N*4-(3-chloro-4-fluoro-phenyl)-*N*4-(3,4-dimethoxy-benzyl)-7-(3-morpholin-4-yl-propoxy)-quinazoline-4,6-diamine;

N-[4-[(3-chloro-4-fluoro-phenyl)-(3,4-dimethoxy-benzyl)-amino]-7-(3-morpholin-4-yl-propoxy)-quinazolin-6-yl]-acrylamide;

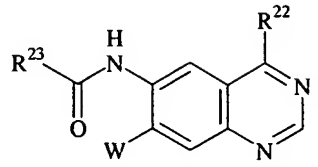
N-(3-chloro-4-fluoro-phenyl)-*N*-[7-(3-morpholin-4-yl-propoxy)-6-nitro-quinazolin-4-yl]-acetamide;

N-[6-amino-7-(3-morpholin-4-yl-propoxy)-quinazolin-4-yl]-*N*-(3-chloro-4-fluoro-phenyl)-acetamide; and

N-[4-[acetyl-(3-chloro-4-fluoro-phenyl)-amino]-7-(3-morpholin-4-yl-propoxy)-quinazolin-6-yl]-acrylamide;

or a pharmaceutically acceptable salt thereof.

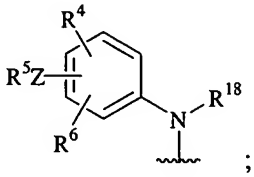
45. A compound of Formula 48,



48

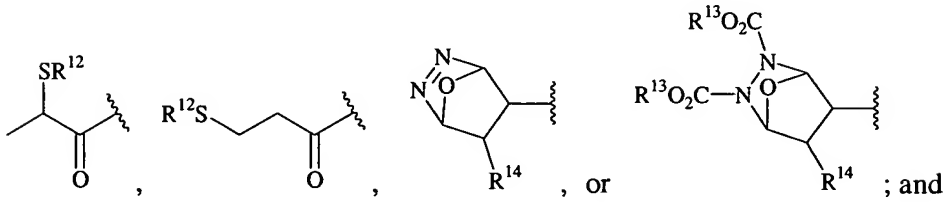
or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof, in which

R^{22} is a leaving group or



;

R^{23} is



; and

W is SR^7, OR^7 or NHR^7;

wherein R^4 and R^6 are independently hydrogen, hydroxy, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkylamino, C_{1-4} alkyldiamino, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylcarbonyl, C_{1-4} alkylcarbamoyl, dicarbamoyl, carbamyl, C_{1-4} alkoxycarbonyl, cyano, nitro, or trifluoromethyl;

R^5 is phenyl, pyridyl, furyl, thiazolyl, imidazolyl or thienyl, each optionally having one or two substituents that are independently halogen, C_{1-6} alkyl, C_{1-6} alkoxy, hydroxy, amino, cyano, C_{1-6} alkyl-NH or $(C_{1-6}$ alkyl$)_2N$;

Z is hydrogen, halogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{1-6} alkoxy, C_{3-8} cycloalkoxy, nitro, C_{1-6} haloalkyl, hydroxy, C_{1-6} acyloxy, NH_2, C_{1-6} alkyl-NH, $(C_{1-6}$ alkyl$)_2N$, C_{3-8} cycloalkyl-NH, $(C_{3-8}$ cycloalkyl$)_2N$, hydroxymethyl, C_{1-6} alkylcarbonyl, cyano, azido, C_{1-6} thioalkyl, C_{1-6} sulfinylalkyl,

C_{1-6} sulfonylalkyl, C_{3-8} thiocycloalkyl, C_{3-8} sulfinylcycloalkyl, C_{3-8} sulfonylcycloalkyl, mercapto, C_{1-6} alkoxycarbonyl, C_{3-8} cycloalkoxycarbonyl, C_{2-4} alkenyl, C_{4-8} cycloalkenyl, or C_{2-4} alkynyl, provided that when Z is monovalent, R^5 is absent;

R^7 is hydrogen, C_{1-6} alkyl, piperidin-1-yl-$(CH_2)_m$, piperazin-1-yl-$(CH_2)_m$, 4-C_{1-6} alkyl-piperazin-1-yl-$(CH_2)_m$, pyrrolidin-1-yl-$(CH_2)_m$, pyridinyl-$(CH_2)_m$, imidazolyl-$(CH_2)_m$, imidazol-1-yl-$(CH_2)_m$, morpholin-4-yl-$(CH_2)_m$, thiomorpholin-4-yl-$(CH_2)_m$, or hexahydroazepin-1-yl-$(CH_2)_m$, wherein each C_{1-6} alkyl optionally includes one or more substituents that are OH, NH_2 or -N(A)B;

R^{12} is C_{1-6} alkyl or aryl;

R^{13} is C_{1-4} alkyl, C_{1-4} haloalkyl, C_{2-4} alkenyl, TMS-$(CH_2)_m$ or aryl-$(CH_2)_m$;

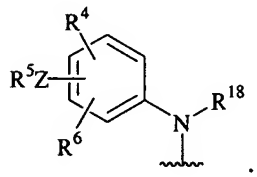
R^{14} is hydrogen, halogen, C_{2-6} alkenyl, C_{2-6} alkynyl, and C_{2-6} alkenyl or C_{2-6} alkynyl substituted with hydroxy, alkoxy, amino or alkylamino;

R^{18} is hydrogen, an O-substituted carbonyldioxy radical, or an S-substituted sulfonyl radical, the O-substituted carbonyldioxy radical or the S-substituted sulfonyl radicals independently substituted with *t*-butyl, allyl, benzyl, *p*-methoxybenzyl, 2-chloroethyl, 2,2,2-trichloroethyl, 2-trimethylsilylethyl, 2-nitroethyl, 2-cyanoethyl, 4-nitrobenzyl, trifluoroacetyl or Tf;

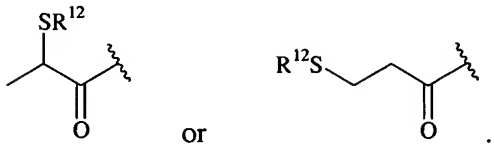
A and B are independently hydrogen, C_{1-6} alkyl, $(CH_2)_mOH$, piperidin-1-yl-$(CH_2)_m$, piperazin-1-yl-$(CH_2)_m$, 4-C_{1-6} alkyl-piperazin-1-yl-$(CH_2)_m$, pyrrolidin-1-yl-$(CH_2)_m$, pyridinyl-$(CH_2)_m$, imidazolyl-$(CH_2)_m$, or imidazol-1-yl-$(CH_2)_m$; and

m is an integer from zero to four, inclusive.

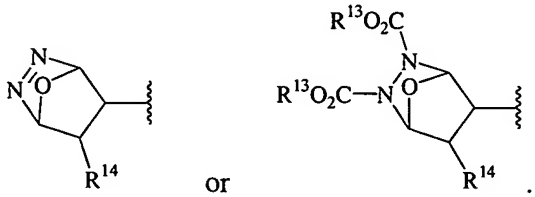
46. The compound of claim 44, wherein R^{22} is



47. The compound of claim 46, wherein R^{18} is hydrogen and R^{23} is

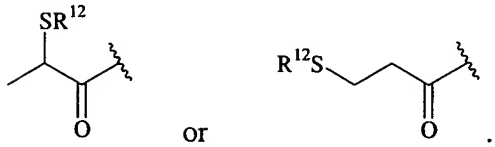


48. The compound of claim 46, wherein R^{18} is hydrogen and R^{23} is

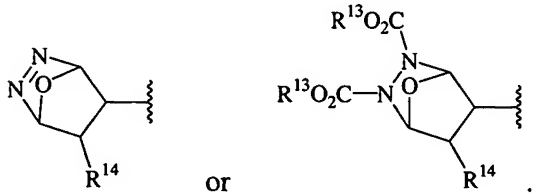


49. The compound of claim 44, wherein R^{22} is a leaving group.

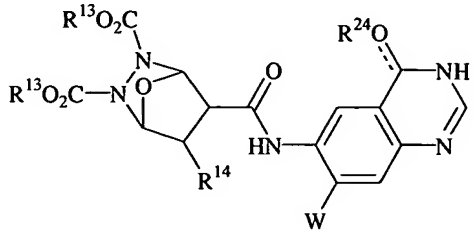
50. The compound of claim 49, wherein R^{18} is hydrogen and R^{23} is



51. The compound of claim 49, wherein R^{18} is hydrogen and R^{23} is



52. A compound of Formula 49,



or a pharmaceutically acceptable salt, ester, amide or prodrug thereof, in which

R^{13} is C_{1-4} alkyl, C_{1-4} haloalkyl, C_{2-4} alkenyl, TMS-$(CH_2)_m$ or aryl-$(CH_2)_m$;

R^{14} is hydrogen, halogen, C_{2-6} alkenyl, C_{2-6} alkynyl, and C_{2-6} alkenyl or C_{2-6} alkynyl substituted with hydroxy, alkoxy, amino or alkylamino;

R^{24} is $P^+(R^{16})_3$ or is absent;

W is SR^7, OR^7 or NHR^7;

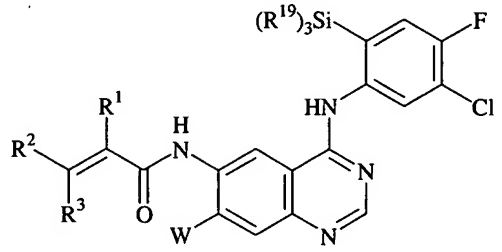
R^7 is hydrogen, C_{1-6} alkyl, piperidin-1-yl-$(CH_2)_m$, piperazin-1-yl-$(CH_2)_m$, 4-C_{1-6} alkyl-piperazin-1-yl-$(CH_2)_m$, pyrrolidin-1-yl-$(CH_2)_m$, pyridinyl-$(CH_2)_m$, imidazolyl-$(CH_2)_m$, imidazol-1-yl-$(CH_2)_m$, morpholin-4-yl-$(CH_2)_m$, thiomorpholin-4-yl-$(CH_2)_m$, or hexahydroazepin-1-yl-$(CH_2)_m$, wherein each C_{1-6} alkyl optionally includes one or more substituents that are OH, NH_2 or -N(A)B;

R^{16} is C_{1-6} alkyl, phenyl, or phenoxy;

A and B are independently hydrogen, C_{1-6} alkyl, $(CH_2)_mOH$, piperidin-1-yl-$(CH_2)_m$, piperazin-1-yl-$(CH_2)_m$, 4-C_{1-6} alkyl-piperazin-1-yl-$(CH_2)_m$, pyrrolidin-1-yl-$(CH_2)_m$, pyridinyl-$(CH_2)_m$, imidazolyl-$(CH_2)_m$, or imidazol-1-yl-$(CH_2)_m$; and

m is an integer from zero to four, inclusive.

53. A compound of Formula 45,



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or a pharmaceutically acceptable salt, ester, amide or prodrug thereof, in which

R^1, R^2 and R^3 are independently hydrogen, halogen, NO_2, CN, CF_3, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-8} cycloalkyl, C_{3-8} heterocyclyl, carboxy, C_{1-6} alkoxycarbonyl, C_{1-6} alkylcarbamoyl, aryl-$(CH_2)_m$, heteroaryl-$(CH_2)_m$, heterocyclyl-$(CH_2)_m$, $(CH_2)_mCO_2R^8$, $(CH_2)_mS(O)_nR^8$, $(CH_2)_mSO_2NR^8R^9$, OR^8, SR^8, $(CH_2)_mNR^8R^9$, $(CH_2)_mN(O)R^8R^9$,

$(CH_2)_mP(O)(OR^8)(OR^9)$, $(CH_2)_mCOR^8$, $(CH_2)_mCO_2R^8$, $(CH_2)_mC(O)NR^8R^9$, $(CH_2)_mC(O)NR^8SO_2R^8$, $(CH_2)_mNR^8SO_2R^9$, $(CH_2)_mC(O)NR^8OR^9$, $(CH_2)_mS(O)_nR^8$, or $(CH_2)_mSO_2NR^8R^9$, wherein aryl-$(CH_2)_m$ includes phenylalkyl or substituted phenylalkyl having from one to three substituents that are independently NO_2, CN, CF_3, C_{1-6} alkyl-NH, $(C_{1-6}$ alkyl$)_2N$, or monocyclic heteroaryl, and each C_{1-6} alkyl is optionally substituted with OH, NH_2 or -N(A)B;

R^{19} is C_{1-4} alkyl, C_{1-4} alkoxy or aryl;

W is SR^7, OR^7 or NHR^7; and

wherein, R^7 is hydrogen, C_{1-6} alkyl, piperidin-1-yl-$(CH_2)_m$, piperazin-1-yl-$(CH_2)_m$, 4-C_{1-6} alkyl-piperazin-1-yl-$(CH_2)_m$, pyrrolidin-1-yl-$(CH_2)_m$, pyridinyl-$(CH_2)_m$, imidazolyl-$(CH_2)_m$, imidazol-1-yl-$(CH_2)_m$, morpholin-4-yl-$(CH_2)_m$, thiomorpholin-4-yl-$(CH_2)_m$, or hexahydroazepin-1-yl-$(CH_2)_m$, wherein each C_{1-6} alkyl optionally includes one or more substituents that are OH, NH_2 or -N(A)B;

R^8 and R^9 are each independently hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, arylalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, or heteroarylalkyl;

A and B are independently hydrogen, C_{1-6} alkyl, $(CH_2)_mOH$, piperidin-1-yl-$(CH_2)_m$, piperazin-1-yl-$(CH_2)_m$, 4-C_{1-6} alkyl-piperazin-1-yl-$(CH_2)_m$, pyrrolidin-1-yl-$(CH_2)_m$, pyridinyl-$(CH_2)_m$, imidazolyl-$(CH_2)_m$, or imidazol-1-yl-$(CH_2)_m$; and

n and m are, respectively, integers from zero to two, inclusive, and from zero to four, inclusive.

54. The compound of claim 53, wherein R^1, R^2 and R^3 are each hydrogen.

55. The compound of claim 53, wherein W is morpholin-4-yl-alkoxy.